

**Article title:** Pragmatic study of a thromboprophylaxis algorithm in critically ill patients with sars-cov-2 infection

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## Results

It was also important to analyze the similarities between the compared groups. There are a number of points to clarify. First, lower ATIII activity D+1 (without statistical significance) in the CG could constitute a pro-thrombotic factor. In our study, when we looked for acquired causes of ATIII deficiency, we found that none were shown to be meaningful between groups at D+1 and the probability of having a congenital ATIII deficit was improbable because of its rarity [S1]. In addition, all other studies have reported normal or marginally reduced ATIII activity on admission to the ICU [42, 45, 46, 47, 57]. Han et al. have demonstrated the absence of difference in ATIII activity in three groups of patients stratified according to the severity of the clinical phenotype of the SARS-CoV-2 infection [6]. In our study, to explain this difference, the most likely hypothesis remains the non-performance of ATIII D+1 measurement in all patients due to the need to request ATIII analysis only in the presence of one of the two other prothrombotic factors mentioned in our algorithm. For more detailed information about the practical use of the algorithm, refer to supplementary file "Online Resource 1".

Second, one might assume that CG patients are more likely to be more "seriously ill" than PG patients because of a higher level of D-dimers on D+1 (not statistically significant). Several studies have suggested that the severity of COVID-19 can be estimated by D-dimer levels on D+1 [1-3, 5, S2]. For example, in the study by Tang et al. the D-dimer level of non-survivors was 2120 ng/mL [3]. In another example, a retrospective multicenter study (5 US healthcare institutions), showed that, in critically ill patients, elevated D-dimer level at initial presentation was predictive of coagulation-associated complications (D-dimer > 2500 ng/mL, adjusted odds ratio [OR] for thrombosis, 6.79 [95% CI, 2.39-19.30]) [S2]. However, debate regarding the appropriate D-dimer threshold and clinical outcome has polarized experts [58, 59, S3, S4].

Third, taken together these arguments rule out heterogeneity, at baseline, between the two groups regarding thrombotic profile. We have presented considerable data concerning demographic, clinical, and biological characteristics confirming the similarity of the two groups, on D+1, with regard to thrombotic risk.

## REFERENCES

S1. Anderson JA, Weitz JI (2011) Hypercoagulable states. *Crit Care Clin*;27(4):933-52, vii.

<https://doi.org/10.1016/j.ccc.2011.09.007>

- S2. Al-Samkari H, Karp Leaf RS, Dzik WH et al (2020) COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. *Blood*;136(4):489-500. <https://doi.org/10.1182/blood.2020006520>.
- S3. Lippi G, Favaloro EJ (2020) D-dimer is associated with severity of coronavirus disease 2019: a pooled analysis. *Thromb Haemost*;120(5):876-78. <https://doi.org/10.1055/s-0040-1709650>
- S4. Hardy M, Lecompte T, Douxfils J et al (2020) Management of the thrombotic risk associated with COVID-19: guidance for the hemostasis laboratory. *Thromb J* 18:17. <https://doi.org/10.1186/s12959-020-00230-1>